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Remington's Pharmaceutical Sciences

18

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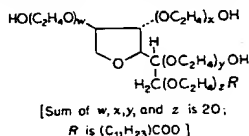
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Printed in the United States of America by the Mack Printing Company, Easton, Pennsylvania

Uses—Contains ester and alcohol functions that impart both lyophilic and hydrophilic characteristics to make it useful as a surfactant and emulsifier. It is an ingredient of some water-soluble ointment and cream bases.

Polysorbates

Sorbitan esters, poly(oxy-1,2-ethanediyl) derivs, Monitans (*Ives-Cameron*); Sorlates (*Abbott*); Tweens (*ICI*)



Sorbitan esters, polyoxyethylene derivatives; fatty acid esters of sorbitol and its anhydrides copolymerized with a varying number of moles of ethylene oxide. The NF recognizes: *Polysorbate 20* (structure given above), a laurate ester; *Polysorbate 40*, a palmitate ester; *Polysorbate 60*, a mixture of stearate and palmitate esters; and *Polysorbate 80*, an oleate ester.

Preparation—These important nonionic surfactants (page 268) are prepared starting with sorbitol by (1) elimination of water-

forming sorbitan (a cyclic sorbitol anhydride); (2) partial esterification of the sorbitan with a fatty acid such as oleic or stearic acid yielding a hexitan ester known commercially as a *Span* and (3) chemical addition of ethylene oxide yielding a *Tween* (the polyoxyethylene derivative).

Description—*Polysorbate 80*: Lemon- to amber-colored, oily liquid; faint, characteristic odor; warm, somewhat bitter taste; specific gravity 1.07 to 1.09; pH (1:20 aqueous solution) 6 to 8.

Solubility—*Polysorbate 80*: Very soluble in water, producing an odorless and nearly colorless solution; soluble in alcohol, cottonseed oil, corn oil, ethyl acetate, methanol or toluene; insoluble in mineral oil.

Uses—Because of their hydrophilic and lyophilic characteristics, these nonionic surfactants are very useful as emulsifying agents forming O/W emulsions in pharmaceuticals, cosmetics and other types of products. *Polysorbate 80* is an ingredient in *Coal Tar Ointment* and *Solution*. See *Glycol Ethers* (page 1313).

Other Water-Soluble Ointment Base Component

Polyethylene Glycol 400 Monostearate USP XVI—An ether, alcohol and ester. Semitransparent, whitish, odorless or nearly odorless mass; melts from 30 to 34°. Freely soluble in carbon tetrachloride, chloroform, ether or petroleum benzin; slightly soluble in alcohol; insoluble in water. **Uses**: A nonionic surface-active agent in the preparation of creams, lotions, ointments and similar pharmaceutical preparations, which are readily soluble in water.

Pharmaceutical Solvents

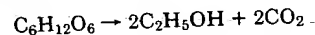
Alcohol

Ethanol; Spiritus Vini Rectificatus; S. V. R.; Spirit of Wine; Methylcarbinol

Ethyl alcohol [64-17-5]; contains 92.3 to 93.8%, by weight (94.9 to 96.0%, by volume), at 15.56° (60°F) of C_2H_5OH (46.07°).

Preparation—Has been made for centuries by fermentation of certain carbohydrates in the presence of *zymase*, an enzyme present in yeast cells. Usable carbohydrate-containing materials include molasses, sugar cane, fruit juices, corn, barley, wheat, potato, wood and waste sulfite liquors. As yeast is capable of fermenting only D-glucose, D-fructose, D-mannose and D-galactose it is essential that more complex carbohydrates, such as starch, be converted to one or more of these simple sugars before they can be fermented. This is accomplished variously, commonly by enzyme- or acid-catalyzed hydrolysis.

The net reaction that occurs when a hexose, glucose for example, is fermented to alcohol may be represented as



but the mechanism of the process is very complex. The fermented liquid, containing about 15% of alcohol, is distilled to obtain a distillate containing 94.9% of C_2H_5OH , by volume. To produce *absolute alcohol*, the 95% product is dehydrated by various processes.

It may be produced also by hydration of ethylene, abundant supplies of which are available from natural and coke oven gases, from waste gases of the petroleum industry and other sources. In another synthesis acetylene is hydrated catalytically to acetaldehyde, which then is hydrogenated catalytically to ethyl alcohol.

Description—Transparent, colorless, mobile, volatile liquid; slight but characteristic odor; burning taste; boils at 78° but volatilizes even at a low temperature, and is flammable; when pure, it is neutral towards all indicators; specific gravity at 15.56° (the US Government standard temperature for Alcohol) not above 0.816, indicating not less than 92.3% of C_2H_5OH by weight or 94.9% by volume.

Solubility—Miscible with water, acetone, chloroform, ether or many other organic solvents.

Incompatibilities—This and preparations containing a high percentage of alcohol will precipitate many inorganic salts from an aqueous solution. *Acacia* generally is precipitated from a hydroalcoholic medium when the alcohol content is greater than about 35%.

Strong oxidizing agents such as *chlorine*, *nitric acid*, *permanganate* or *chromate* in acid solution react, in some cases violently, with it to produce oxidation products.

Alkalies cause a darkening in color due to the small amount of aldehyde usually present in it.

The remarkable growth of the solvent industry is attested by the more than 300 solvents now being produced on an industrial scale. Chemically, these include a great variety of organic compounds, ranging from hydrocarbons through alcohols, esters, ethers and acids to nitroparaffins. Their main applications are in industry and the synthesis of organic chemicals. Comparatively few, however, are used as solvents in pharmacy, because of their toxicity, volatility, instability and/or flammability. Those commonly used as pharmaceutical solvents are described in this section.

Acetone

2-Propanone; Dimethyl Ketone



Acetone [67-64-1] C_3H_6O (58.08°).

Caution—It is very flammable. Do not use where it may be ignited.

Preparation—Formerly obtained exclusively from the destructive distillation of wood. The distillate, consisting principally of methanol, acetic acid and acetone was neutralized with lime and the acetone was separated from the methyl alcohol by fractional distillation. Additional quantities were obtained by pyrolysis of the calcium acetate formed in the neutralization of the distillate.

It now is obtained largely as a by-product of the butyl alcohol industry. This alcohol is formed in the fermentation of carbohydrates such as corn starch, molasses, etc, by the action of the bacterium *Clostridium acetobutylicum* (Weizmann fermentation) and it is always one of the products formed in the process. It also is obtained by the catalytic oxidation of isopropyl alcohol, which is prepared from propylene resulting from the "cracking" of crude petroleum.

Description—Transparent, colorless, mobile, volatile, flammable liquid with a characteristic odor; specific gravity not more than 0.789; distills between 55.5 and 57°; congeals about -95°; aqueous solution neutral to litmus.

Solubility—Miscible with water, alcohol, ether, chloroform or most volatile oils.

Uses—An *antiseptic* in concentrations above 80%. In combination with alcohol it is used as an antiseptic *cleansing solution*. It is employed as a *menstruum* in the preparation of oleoresins in place of ether. It is used as a *solvent* for dissolving fatty bodies, resins, pyroxylin, mercurials, etc, and also in the manufacture of many organic compounds such as chloroform, chlorobutanol and ascorbic acid.

Uses—In pharmacy principally for its solvent powers (page 216). It also is used as the starting point in the manufacture of many important compounds, like ether, chloroform, etc. It also is used as a fuel, chiefly in the denatured form.

It is a CNS depressant. Consequently, it occasionally has been administered intravenously for preoperative and postoperative sedation in patients in whom other measures are ineffective or contraindicated. The dose employed is 1 to 1.5 mL/kg. Its intravenous use is a specialized procedure and should be employed only by one experienced in the technique of such use.

It is used widely and abused by lay persons as a sedative. It has, however, no medically approved use for this purpose. Moreover, alcohol potentiates the CNS effects of numerous sedative and depressant drugs. Hence, it should not be used by patients taking certain prescription drugs or OTC medications (see page 1852).

Externally, it has a number of medical uses. It is a solvent for the toxicodendrol causing *ivy poisoning*, and should be used to wash the skin thoroughly soon after contact. In a concentration of 25% it is employed for bathing the skin for the purpose of *cooling and reducing fevers*. In high concentrations it is a *rubefacient* and an ingredient of many liniments. In a concentration of 50% it is used to prevent sweating in *astrigent and anhidrotic* lotions. It also is employed to cleanse and harden the skin and is helpful in preventing *bedsores* in bedridden patients. In a concentration of 60 to 90% it is germicidal. At optimum concentration (70% by weight) it is a good *antiseptic* for the skin (*local anti-infective*) and also for instruments. It also is used as a *solvent* to cleanse the skin splashed with phenol. High concentrations of it often are injected into nerves and ganglia for the *relief of pain*, accomplishing this by causing nerve degeneration.

Denatured Alcohol

An act of Congress June 7, 1906, authorizes the withdrawal of alcohol from bond without the payment of internal revenue tax, for the purpose of denaturation and use in the arts and industries. This is ethyl alcohol to which have been added such denaturing materials as to render the alcohol unfit for use as an intoxicating beverage. It is divided into two classes, namely, *completely denatured alcohol* and *specially denatured alcohol*, prepared in accordance with approved formulas prescribed in Federal Industrial Alcohol Regulations 3.

Information regarding the use of alcohol and permit requirements may be obtained from the Regional Director, Bureau of Alcohol, Tobacco and Firearms, in any of the following offices: Cincinnati, OH; Philadelphia, PA; Chicago, IL; New York, NY; Atlanta, GA; Dallas, TX and San Francisco, CA. Federal regulation provides that completely and specially denatured alcohols may be purchased by properly qualified persons from duly established denaturing plants or bonded dealers. No permit is required for the purchase and use of completely denatured alcohol unless the purchaser intends to recover the alcohol.

Completely Denatured Alcohol—This term applies to ethyl alcohol to which has been added materials (methyl isobutyl ketone, pyronate, gasoline, acetaldol, kerosene, etc) of such nature that the products may be sold and used within certain limitations without permit and bond.

Specially Denatured Alcohol—This alcohol is intended for use in a greater number of specified arts and industries than completely denatured alcohol and the character of the denaturant or denaturants used is such that specially denatured alcohol may be sold, possessed and used only by those persons or firms that hold basic permits and are covered by bond.

Formulas for products using specially denatured alcohol must be approved prior to use by the Regional Director, Bureau of Alcohol, Tobacco and Firearms in any of the regional offices listed above.

Uses—Approximately 50, specially denatured alcohol formulas containing combinations of more than 90 different denaturants are available to fill the needs of qualified users. Large amounts of specially denatured alcohols are used as raw materials in the production of acetaldehyde, synthetic rubber, vinegar and ethyl chloride as well as in the manufacture of proprietary solvents and cleaning solutions. Ether and chloroform can be made from suitably denatured alcohols and formulas for the manufacture of Iodine Tincture, Green Soap Tincture and Rubbing Alcohol are set forth in the regulations.

Specially denatured alcohols also are used as solvents for surface coatings, plastics, inks, toilet preparations and external pharmaceu-

tics. Large quantities are used in the processing of such food and drug products as pectin, vitamins, hormones, antibiotics, alkaloids and blood products. Other uses include supplemental motor fuel, rocket and jet fuel, antifreeze solutions, refrigerants and cutting oils. Few products are manufactured today that do not require the use of alcohol at some stage of production. Specially denatured alcohol may not be used in the manufacture of foods or internal medicines where any of the alcohol remains in the finished product.

Rose Water Ointment

Cold Cream; Galen's Cerate

Cetyl Esters Wax	125 g
White Wax	120 g
Almond Oil	560 g
Sodium Borate	5 g
Stronger Rose Water	25 mL
Purified Water	165 mL
Rose Oil	0.2 mL
To make about	1000 g

Reduce the cetyl esters wax and the white wax to small pieces, melt them on a steam bath, add the almond oil and continue heating until the temperature of the mixture reaches 70°. Dissolve the sodium borate in the purified water and stronger rose water, warmed to 70°, and gradually add the warm solution to the melted mixture, stirring rapidly and continuously until it has cooled to about 45°. Incorporate the rose oil.

It must be free from rancidity. If the ointment has been chilled, warm it slightly before attempting to incorporate other ingredients (see USP for allowable variations).

History—Originated by Galen, the famous Roman physician-pharmacist of the 1st century AD, was known for many centuries by the name of *Unguentum* or *Ceratum Refrigerans*. It has changed but little in proportions or method of preparation throughout many centuries.

Uses—An *emollient* and *ointment base*. It is a W/O emulsion.

Diluted Alcohol

Diluted Ethanol

A mixture of alcohol and water containing 41.0 to 42.0%, by weight (48.4 to 49.5%, by volume), at 15.56°, of C₂H₅OH (46.07).

Preparation—

Alcohol	500 mL
Purified Water	500 mL

Measure the alcohol and the purified water separately at the same temperature, and mix. If the water and the alcohol and the resulting mixture are measured at 25°, the volume of the mixture will be about 970 mL.

When equal volumes of alcohol and water are mixed together, a rise in temperature and a contraction of about 3% in volume take place. In small operations the contraction generally is disregarded; in larger operations it is very important. If 50 gal of official alcohol are mixed with 50 gal of water, the product will not be 100 gal of diluted alcohol, but only 96¼ gal, a contraction of 3¾ gal. US *Proof Spirit* differs from this and is stronger; it contains 50%, by volume, of absolute alcohol at 15.56° (60°F). This corresponds to 42.5% by weight, and has a specific gravity of 0.9341 at the same temperature. If spirits have a specific gravity lower than that of "proof spirit" (0.9341), they are said to be "*above proof*," if greater, "*below proof*." It also may be prepared from the following:

Alcohol	408 g
Purified Water	500 g

Rules for Dilution—The following rules are applied when making an alcohol of any required lower percentage from an alcohol of any given higher percentage:

I. **By Volume**—Designate the volume percentage of the stronger alcohol by *V*, and that of the weaker alcohol by *v*.

Rule—Mix *v* volumes of the stronger alcohol with purified water to make *V* volumes of product. Allow the mixture to stand until full contraction has taken place, and until it has cooled, then make up the deficiency in the *V* volumes by adding more purified water.

Example—An alcohol of 30% by volume is to be made from an alcohol of 94.9% by volume.—Take 30 volumes of the 94.9% alcohol, and add enough purified water to produce 94.9 volumes at room temperature.

II. By Weight—Designate the weight-percentage of the stronger alcohol by *W*, and that of the weaker alcohol by *w*.

Rule—Mix *w* parts by weight of the stronger alcohol with purified water to make *W* parts by weight of product.

Example—An alcohol of 50% by weight is to be made from an alcohol of 92.3% by weight.—Take 50 parts by weight of the 92.3% alcohol, and add enough purified water to produce 92.3 parts by weight.

Description—As for *Alcohol*, except its specific gravity is 0.935 to 0.937 at 15.56°, indicating that the strength of C_2H_5OH corresponds to that given in the official definition.

Uses—A menstruum in making tinctures, fluidextracts, extracts, etc. Its properties already have been described fully in connection with the various preparations. Its value consists not only in its *antiseptic* properties, but also in its possessing the *solvent* powers of both water and alcohol. See *Alcohol*.

Nonbeverage Alcohol

This is tax-paid alcohol or distilled spirits used in the manufacture, by approved formula, of such medicines, medicinal preparations, food products, flavors or flavoring extracts as are unfit for beverage purposes. Internal Revenue Service Regulations provide that qualified holders of Special Tax Stamps who use tax paid alcohol or distilled spirits in the types of products listed above, may file a claim for *alcohol tax drawback* or refund of a considerable part of the tax paid.

Amylene Hydrate

2-Butanol, 2-methyl-, Tertiary Amyl Alcohol; Dimethylethylcarbinol



tert-Pentyl alcohol [75-85-4] $C_5H_{12}O$ (88.15).

Preparation—Amylene is mixed with 2 volumes of 60% H_2SO_4 , both previously cooled to 0°, for about 1 hr; then neutralized with soda, distilled and the first half of the distillate containing most of the amylene hydrate is treated with anhydrous potassium carbonate and redistilled.

Description—Clear, colorless liquid of camphoraceous odor; solution neutral to litmus; specific gravity 0.803 to 0.807; distills completely between 97 and 103°.

Solubility—1 g in about 8 mL of water; miscible with alcohol, chloroform, ether or glycerin.

Uses—Chiefly, a *pharmaceutic necessity* for *Tribromoethanol Solution* (RPS-15, page 985). It has been used as a *sedative-hypnotic* in doses of 1 to 4 g administered in glycerin.

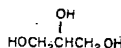
Chloroform—page 1320.

Ether—page 1041.

Ethyl Acetate—page 1294.

Glycerin

1,2,3-Propanetriol; Glycerol

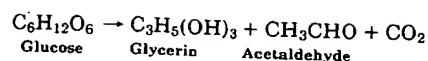


Glycerol [56-81-5] $C_3H_8O_3$ (92.09).

Chemically, it is the simplest trihydric alcohol. It is worthy of special note because the two terminal alcohol groups are primary, whereas the middle one is secondary. Thus this becomes the first polyhydric alcohol which can yield both an aldose (*glyceraldehyde*) and a ketose (*dihydroxyacetone*).

Preparation—

1. By saponification of fats and oils in the manufacture of soap.
2. By hydrolysis of fats and oils through pressure and superheated steam.
3. By fermentation of beet sugar molasses in the presence of large amounts of sodium sulfite. Under these conditions a reaction takes place expressed as



4. Glycerin is now prepared in large quantities from propylene, a petroleum product. This hydrocarbon is chlorinated at about 400° to form allyl chloride, which is converted to allyl alcohol. Treatment of the unsaturated alcohol with hypochlorous acid [$HOCl$] yields the chlorohydrin derivative. Extraction of HCl with soda lime yields 2,3-epoxypropanol which undergoes hydration to glycerin.

Description—Clear, colorless, syrupy liquid with a sweet taste and not more than a slight, characteristic odor, which is neither harsh nor disagreeable; when exposed to moist air it absorbs water and also such gases as H_2S and SO_2 ; solutions are neutral; specific gravity not below 1.249 (not less than 95% $C_3H_5(OH)_3$); boils at about 290° under 1 atm, with decomposition, but can be distilled intact in a vacuum.

Solubility—Miscible with water, alcohol methanol; 1 g in about 12 mL of ethyl acetate or about 15 mL of acetone; insoluble in chloroform, ether or fixed and volatile oils.

Incompatibilities—An explosion may occur if it is triturated with strong oxidizing agents such as *chromium trioxide*, *potassium chlorate* or *potassium permanganate*. In dilute solutions the reactions proceed at a slower rate forming several oxidation products. Iron is an occasional contaminant of it and may be the cause of a darkening in color in mixtures containing *phenols*, *salicylates*, *tannin*, etc.

With *boric acid* or *sodium borate*, it forms a complex, generally spoken of as glyceroboric acid, which is a much stronger acid than boric acid.

Uses—One of the most valuable products known to pharmacy by virtue of its *solvent* property. It is useful as a *humectant* in keeping substances moist, owing to its hygroscopicity. Its agreeable taste and high viscosity adapt it for many purposes. Some modern ice collars and ice bags contain it and water hermetically sealed within vulcanized rubber bags. The latter are sterilized by dipping in a germicidal solution and are stored in the refrigerator until needed. It also has some therapeutic uses. In pure anhydrous form, it is used in the eye to reduce corneal edema and to facilitate ophthalmoscopic examination. It is used orally as an evacuant and, in 50 to 75% solution, as a systemic osmotic agent.

Isopropyl Alcohol—page 1167.

Methyl Alcohol

Methanol; Wood Alcohol



Methanol [67-56-1] CH_4O (32.04).

Caution—It is *poisonous*.

Preparation—By the catalytic reduction of carbon monoxide or carbon dioxide with hydrogen. A zinc oxide-chromium oxide catalyst is used commonly.

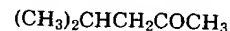
Description—Clear, colorless liquid; characteristic odor; flammable; specific gravity not more than 0.790; distills within a range of 1° between 63.5 and 65.7°.

Solubility—Miscible with water, alcohol, ether, benzene or most other organic solvents.

Uses—A *pharmaceutic aid* (solvent). It is toxic. Ingestion may result in blindness; vapors also may cause toxic reactions.

Methyl Isobutyl Ketone

2-Pentanone, 4-methyl-,



4-Methyl-2-pentanone [108-10-1]; contains not less than 99% of $C_6H_{12}O$ (100.16).

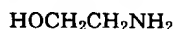
Description—Transparent, colorless, mobile, volatile liquid; faint, ketonic and camphoraceous odor, distills between 114 and 117°.

Solubility—Slightly soluble in water; miscible with alcohol, ether or benzene.

Uses—A *denaturant* for rubbing alcohol and also a *solvent* for gums, resins, nitrocellulose, etc. It may be irritating to the eyes and mucous membranes, and, in high concentrations, narcotic.

M noethanolamin

Ethanol, 2-amino-, Ethanolamine; Ethylolamine

2-Aminoethanol [141-43-5] $\text{C}_2\text{H}_7\text{NO}$ (61.08).**Preparation**—This alkanolamine is prepared conveniently by treating ethylene oxide with ammonia.**Description**—Clear, colorless, moderately viscous liquid; distinctly ammoniacal odor; affected by light; specific gravity 1.013 to 1.016; distills between 167 and 173°.**Solubility**—Miscible in all proportions with water, acetone, alcohol, glycerin or chloroform; immiscible with ether, solvent hexane or fixed oils; dissolves many essential oils.**Uses**—A solvent for fats, oils and many other substances, it is a pharmaceutical necessity for *Thimerosal Solution* (page 1173). It combines with fatty acids to form soaps which find application in various types of emulsions such as lotions, creams, etc.**Propylene Glycol**1,2-Propanediol [57-55-6] $\text{C}_3\text{H}_8\text{O}_2$ (76.10).**Preparation**—Propylene is converted successively to its chlorohydrin (with HOCl), epoxide (with Na_2CO_3) and glycol (with water in presence of protons).**Description**—Clear, colorless, viscous and practically odorless liquid; slightly acid taste; specific gravity 1.035 to 1.037; completely distills between 184 and 189°; absorbs moisture from moist air.**Solubility**—Miscible with water, alcohol, acetone or chloroform; soluble in ether; dissolves many volatile oils; immiscible with fixed oils.**Uses**—A solvent, preservative and humectant. See *Hydrophilic Ointment* (page 1311).**Trolamine**

Ethanol, 2,2',2''-nitrilotris-, Triethanolamine.

Miscellaneous Pharmaceutical Necessities

The agents listed in this section comprise a heterogeneous group of substances with both pharmaceutical and industrial applications. Pharmaceutically, some of these agents are used as diluents, enteric coatings, excipients, filtering agents and as ingredients in products considered in other chapters. Industrially, some of these agents are used in various chemical processes, in the synthesis of other chemicals and in the manufacture of fertilizers, explosives, etc.

Acetic AcidAcetic acid; a solution containing 36 to 37%, by weight, of $\text{C}_2\text{H}_4\text{O}_2$ (60.05).**Preparation**—By diluting with distilled water an acid of higher concentration, such as the 80% product, or more commonly glacial acetic acid, using 350 mL of the latter for the preparation of each 1000 mL of acetic acid.**Description**—Clear, colorless liquid, having a strong characteristic odor and a sharply acid taste; specific gravity about 1.045; congeals about -14°; acid to litmus.**Solubility**—Miscible with water, alcohol or glycerin.**Uses**—In pharmacy as a solvent and menstruum, and for making diluted acetic acid. It also is used as a starting point in the manufacture of many other organic compounds, eg, acetates, acetanilid, sulfonamides, etc. It is official primarily as a pharmaceutical necessity for the preparation of *Aluminum Subacetate Solution* (RPS-17, page 778).**Diluted Acetic Acid**

Dilute Acetic Acid

2,2',2''-Nitrilotriethanol [102-71-6] $\text{N}(\text{C}_2\text{H}_4\text{OH})_3$ (149.19); a mixture of alkanolamines consisting largely of triethanolamine, containing some diethanolamine [$\text{NH}(\text{C}_2\text{H}_4\text{OH})_2$ = 105.14] and monoethanolamine [$\text{NH}_2\text{C}_2\text{H}_4\text{OH}$ = 61.08].**Preparation**—Along with some mono- and diethanolamine, by the action of ammonia on ethylene oxide.**Description**—Colorless to pale yellow, viscous, hygroscopic liquid; slight odor of ammonia; aqueous solution is very alkaline; melts about 21°; specific gravity 1.120 to 1.128; a strong base and readily combines even with weak acids to form salts.**Solubility**—Miscible with water or alcohol; soluble in chloroform; slightly soluble in ether or benzene.**Uses**—In combination with a fatty acid, eg, oleic acid (see *Benzyl Benzoate Lotion*, page 1246), as an emulsifier. See *Monoethanolamine*.**Water**—page 1300.**Other Pharmaceutical Solvents****Alcohol, Dehydrated, BP, PhI** [Dehydrated Ethanol; Absolute Alcohol]—Transparent, colorless, mobile, volatile liquid; characteristic odor; burning taste; specific gravity not more than 0.798 at 15.56°; hygroscopic, flammable and boils about 78°C. Miscible with water, ether or chloroform. **Uses:** A pharmaceutical solvent; also used by injection for relief of pain (see *Alcohol*, page 1314).**Coconut Oil** [Coconut Oil; Copra Oil]—The fixed oil obtained by expression or extraction from the kernels of the seeds of *Cocos nucifera* Linné (Fam *Palmae*). Pale yellow to colorless liquid between 28 and 30°, semisolid at 20° and a hard, brittle crystalline solid below 15°; odorless and tasteless or has a faint odor and taste characteristic of coconut; it must not be used if it has become rancid; melts about 23°; specific gravity 0.918 to 0.923. Readily soluble in alcohol, ether, chloroform, carbon disulfide or petroleum benzin; insoluble in water.**Petroleum Benzin** [Petroleum ether; Purified benzin]—Clear, colorless, volatile liquid; ethereal or faint, petroleum-like odor; neutral reaction; specific gravity 0.634 to 0.660. Practically insoluble in water; miscible with ether, chloroform, benzene or fixed oils. **Caution:** Highly flammable, and its vapor, when mixed with air and ignited, may explode. **Uses:** A solvent for fats, resins, oils and similar substances.A solution containing, in each 100 mL, 5.7 to 6.3 g of $\text{C}_2\text{H}_4\text{O}_2$.**Preparation**—

Acetic Acid 158 mL

Purified Water, a sufficient quantity,

To make 1000 mL

Mix the ingredients.

Note—This acid also may be prepared by diluting 58 mL of glacial acetic acid with sufficient purified water to make 1000 mL.**Description**—Essentially the same properties, solubility, purity and identification reactions as *Acetic Acid*, but its specific gravity is about 1.008 and it congeals about -2°.**Uses**—*Bactericidal* to many types of microorganisms and occasionally is used in 1% solution for surgical dressings of the skin. A 1% solution is *spermatocidal*. It also is used in vaginal douches for the management of *Trichomonas*, *Candida* and *Hemophilus* infections.**Glacial Acetic Acid**

Concentrated Acetic Acid; Crystallizable Acetic Acid; Ethanolic Acid; Vinegar Acid

Glacial acetic acid [64-19-7] $\text{C}_2\text{H}_4\text{O}_2$ (60.05).**Preparation**—This acid is termed "glacial" because of its solid, glassy appearance when congealed. In one process it is produced by distillation of weaker acids to which has been added a water-entraining substance such as ethylene dichloride. In this method, referred to as "azeotropic distillation," the ethylene dichloride dis-

Add the Veegum, slowly and with continuous stirring, to the syrup. Incorporate the sodium citrate into the Veegum-syrup mixture. Premix the sulfa drugs, add to the syrup, stir and homogenize. Add sufficient 5% citric acid to adjust the pH of the product to 5.6. A preservative and a flavoring agent may be added to the product.

Methods of preparation for those formulations which contain several active ingredients and are produced in large quantities tend to be more complex than that given above.

Many formulations for suspensions are given in the PC under *Mixtures*.

A properly prepared suspension has a number of desirable properties:

1. The suspended material should not settle rapidly.

2. Particles that do settle should not form a hard cake and easily should be resuspended uniformly on shaking.
3. The suspension should pour freely from the container.

Insoluble powders that do not disperse evenly throughout the suspending medium, when shaken, should be powdered finely and levigated with a small amount of an agent such as glycerin, alcohol or a portion of the dispersion of the suspending agent. The other ingredients are incorporated and the remainder of the dispersion of the suspending agent is incorporated gradually by trituration to produce the appropriate volume.

Suspensions intended for parenteral or ophthalmic use also are described in the USP. For a discussion of these suspensions, see Chapter 84 and 86.

Extracts

Extraction

Extraction, as the term is used pharmaceutically, involves the separation of medicinally active portions of plant or animal tissues from the inactive or inert components by using selective solvents in standard extraction procedures.

The products so obtained from plants are relatively impure liquids, semisolids or powders intended only for oral or external use. These include classes of preparations known as decoctions, infusions, fluidextracts, tinctures, pilular (semisolid) extracts and powdered extracts. Such preparations popularly have been called galenicals, after Galen, the 2nd century Greek physician. For additional information concerning extraction and extractives, see RPS 15, Chapter 86.

Extraction continues to be of considerable interest in order to obtain improved yields of drugs derived from plant and animal sources. For example, improved extraction of digitalis glycosides has been carried out using a pulsating, perforated, bottom column. Other techniques include ultrasonics, rotary-film evaporators, liquid and supercritical carbon dioxide, hydrodistillation, liquid chromatography, multiple-solvent extraction, countercurrent extraction and gravitation dynamics.

In this discussion we are concerned primarily with basic extraction procedures for crude drugs to obtain the therapeutically desirable portion and eliminate the inert material by treatment with a selective solvent, known as the menstruum. Extraction differs from solution in that the presence of insoluble matter is implied in the former process. The principal methods of extraction are maceration, percolation, digestion, infusion and decoction. The quality of the finished product can be enhanced by standardizing primary extracts and carrying out analytical assays during production on the raw materials, intermediate products and manufacturing procedures.

The processes of particular importance, insofar as the USP is concerned, are those of maceration and percolation. Most pharmacopeias refer to such processes for extraction of active principles from crude drugs.

Maceration—In this process the solid ingredients are placed in a stoppered container with the whole of the solvent and allowed to stand for a period of at least 3 days, with frequent agitation, until soluble matter is dissolved. The mixture then is strained, the marc (the damp solid material) pressed and the combined liquids clarified by filtration or by decantation, after standing.

Percolation—This is the procedure used most frequently to extract the active ingredients in the preparation of tinctures and fluidextracts. Certain specific procedural details are provided in the USP, which should be consulted for such information. In the PC general procedure, a percolator (a narrow, cone-shaped vessel open at both ends) is used. The solid ingredient(s) are moistened with an appropriate amount of the specified menstruum and allowed to stand for approximately 4 hr in a well-closed container, after which the drug mass is packed into the percolator. Sufficient menstruum is added to saturate the mass and the top of the percolator is closed. When the liquid is about to drip from the neck (bottom) of the percolator, the outlet is closed. Additional menstruum is added to give a shallow layer above the mass, and the mixture is allowed to macerate in the closed percolator for 24 hr. The outlet of the percolator then is opened and the liquid contained therein allowed to drip slowly, additional menstruum being added as required, until the

percolate measures about three-quarters of the required volume of the finished product. The marc is pressed and the expressed liquid is added to the percolate. Sufficient menstruum is added to produce the required volume, and the mixed liquid clarified by filtration or by allowing it to stand and then decanting.

Digestion—This is a form of maceration in which *gentle heat* is used during the process of extraction. It is used when moderately elevated temperature is not objectionable and the solvent efficiency of the menstruum is increased thereby.

Infusion—An infusion is a dilute solution of the readily soluble constituents of crude drugs. Fresh infusions are prepared by macerating the drugs for a short period of time with either cold or boiling water. US official compendia have not included infusions for some time. An example is Concentrated Compound Gentian Infusion BP 1973.

Decoction—This once-popular process extracts water-soluble and heat-stable constituents from crude drugs by boiling in water for 15 min, cooling, straining and passing sufficient cold water through the drug to produce the required volume.

Extractive Preparations

After a solution of the active constituents of a crude drug is obtained by maceration or percolation, it may be ready for use as a medicinal agent, as with certain tinctures or fluidextracts, or it may be processed further to produce a solid or semisolid extract.

For a discussion of *resins* and *oleoresins* obtained by solvent extraction of plant exudates see Chapter 23, under *Plant Exudates*.

Tinctures—Tinctures are defined in the USP as being alcoholic or hydroalcoholic solutions prepared from vegetable materials or from chemical substances, an example of the latter being Iodine Tincture. Traditionally, tinctures of potent vegetable drugs essentially represent the activity of 10 g of the drug in each 100 mL of tincture, the potency being adjusted following assay. Most other tinctures of vegetable drugs represent the extractive from 20 g of the drug in 100 mL of tincture.

The USP specifically describes two general processes for preparing tinctures, one by percolation designated as Process P, and the other by maceration, as Process M. These utilize the methods described under *Extraction*.

Process P includes a modification so that tinctures that require assay for adjustment to specified potency thus may be tested before dilution to final volume. A tincture prepared by Process P as modified for assayed tinctures is *Belladonna Tincture*.

Examples of tinctures prepared by Process M are *Compound Benzoin Tincture* and *Sweet Orange Peel Tincture* (the latter contains the extractive from 50 g of sweet orange peel in 100 mL of tincture).

Fluidextracts—The USP defines fluidextracts as being liquid preparations of vegetable drugs, containing alcohol as a solvent or as a preservative, or both, so made that each mL contains the therapeutic constituents of 1 g of the standard